Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Blistex Cold Sore Cream 100mg/g cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains 100 mg of docosanol.

Excipient: 50 mg propylene glycol/gram cream.
For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Cream
White cream

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of early stages (prodrome or erythema phase) of recurrent labial herpes simplex infection (cold sores) in immunocompetent adults and adolescents (over 12 years old).

4.2 Posology and method of administration

Route of Administration: Cutaneous use

Posology

Adults and adolescents (12-18 years): Apply a thin film carefully over the entire cold sore 5 times a day (approximately every 3 hours during waking hours).
Treatment must begin as soon as possible after the first cold sore symptoms or signs appear (pain, burning/itching/tingling or redness) as efficacy has not been demonstrated when the treatment is initiated at the stage of an already developed blister or ulcer.
Treatment should continue until healing has occurred, usually 4 to 6 days, or for a maximum of 10 days.

Elderly: No special dose recommendation.

Paediatric population
The safety and efficacy of Blistex Cold Sore Cream 100 mg/g in children aged younger than 12 years have not been established (see section 4.4).

Dosage in renal failure: No dose adjustments necessary due to negligible topical absorption.

4.3 Contraindications

Hypersensitivity to the active substance "docosanol" or to any of the excipients.

4.4 Special warnings and precautions for use

Avoid application close to or in the eyes.

This formulation contains propylene glycol and may cause skin irritation. The cream should not be used in immunocompromised patients.

Treatment with the cream should not be initiated at the stage of an already developed blister or ulcer since no efficacy has been demonstrated at this point.

Paediatric population

There is no treatment experience available for the use in children below the age of 12 years and only limited experience in adolescent (aged 12-18 years). It is recommended that the cream should not be used in children under 12 years.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. Therefore, Blistex Cold Sore Cream 100 mg/g cream should not be used simultaneously with other topical products (medicines, cosmetic products, creams) at the same application site.

4.6 Fertility, pregnancy and lactation

Fertility:

There are no adequate data from the use of docosanol on fertility in humans.

Pregnancy

There are no data from the use of docosanol in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development. Since systemic exposure to docosanol is negligible, docosanol can be used during pregnancy.

Lactation

There are no data from the use of docosanol in breast feeding women. No effects on the suckling child are anticipated since the systemic exposure of the breast-feeding

4.7 Effects on ability to drive and use machines

Due to its negligible absorption docosanol has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
not known (cannot be estimated from the available data).

Results from clinical trials of the treatment of recurrent labial herpes simplex demonstrate no difference in the frequency or type of undesirable effects in patients treated with Blistex Cold Sore Cream 100 mg/g cream or placebo.

Nervous system disorders
Very common: Headache (10.4% of docosanol-treated patients and 10.7% of placebo-treated patients).

General disorders and administration site conditions
Common: Application site adverse reactions which include dry skin, rashes and skin disorders (2.9% of docosanol-treated patients and 2.3% of placebo-treated patients).
Facial oedema has also been reported but these application site adverse reactions are consistent with normal facial reactions experienced with cold sores.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: http://www.hpra.ie/; E-mail: medsafety@hpra.ie.

4.9 Overdose

Adverse reactions related to overdose by topical application of Blistex Cold Sore Cream 100 mg/g cream are unlikely because of negligible percutaneous absorption. Similarly, poor oral absorption makes the occurrence of adverse reactions unlikely following ingestion of docosanol.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Chemotherapeutics for topical use, antivirals
ATC code: D06BB11

The exact mechanism of the antiviral activity of docosanol is unknown. *In vitro* studies indicate that docosanol affects the fusion between the virus and the plasma membrane, which inhibits intracellular uptake and replication of virus. *In vitro* studies demonstrate that docosanol-treated cells resist infection by lipid-enveloped viruses such as HSV-1. Docosanol has no effect against non-enveloped viruses.

Docosanol 100 mg/g was compared to placebo (containing polyethylene glycol) in two randomised, double-blind, controlled clinical trials. In one study, 370 adults were randomised. Subjects started with treatment in the prodrome or erythema phase of an acute recurrence of orofacial herpes. The ITT population consisted of 183 subjects for docosanol and 183 subjects for placebo. The median time to complete healing was 4.0 days in the docosanol group and 4.7 days in the placebo group a difference of 18.9 hours (p=0.0235; p=0.010 with covariate adjustment). In the second study, 373 adults were randomised. Subjects started with treatment in the prodrome or erythema phase of an acute recurrence of orofacial herpes. The ITT population consisted of 187 subjects for docosanol and 184 subjects for placebo. The median time to complete healing was 4.3 days in the docosanol group and 4.9 days in the placebo group a difference of 15.9 hours (p=0.1529; p=0,008 with covariate adjustment). In studies with treatment initiation at stages later than the prodromal or erythema stage, efficacy was not demonstrated.

5.2 Pharmacokinetic properties

Under conditions reflecting normal clinical use of Blistex Cold Sore Cream 100 mg/g, docosanol could not be quantified (limit of quantification, LOQ = 10 ng/ml) in the plasma of treated patients. Ten women with active labial herpes simplex were treated with Blistex Cold Sore Cream 100 mg/g. After a single dose on study day 1 and after multiple doses (five times daily, study days 2-3), blood samples were withdrawn up to 24 hours after treatment and analysed for docosanol. Of the 209 plasma samples analysed, the docosanol level was below the LOQ in 208 and exactly at the LOQ in one sample.
Docosanol is metabolized to docosanoic acid, its major metabolite. Both docosanol and docosanoic acid are endogenous components of cell membranes in man, particularly in erythrocytes, brain, nerve myelin sheath, lung, and

kidney.

5.3 Preclinical safety data

Preclinical data revealed no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose stearates (mono and distearate)
Light mineral oil
Propylene glycol
Benzyl alcohol
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.
After first opening the container: 6 months.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Epoxy-lined aluminium tubes closed with a polyethylene screw cap.
Pack sizes: 2 g, 2 g with transparent protective case, 5 g, and 15 g
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

DDD Ltd
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8 MARKETING AUTHORISATION NUMBER

PA0302/012/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22nd June 2007
Date of last renewal: 14th November 2008

10 DATE OF REVISION OF THE TEXT

May 2017